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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/462,816	LI ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/16/03*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Final Rejection

Claims 1-9 and 14-15 are pending examination.

Applicants' traversal, the amendment to claim 1, and the cancellation of claims 15-49 in paper no. filed on 10/16/03 is acknowledged and considered.

Drawings

The drawings were received on 10/16/03. These drawings are acceptable.

Response to Arguments

Applicant's arguments, see, filed 10/16/03, with respect to objection have been fully considered and are persuasive. The rejection of claim 1 has been withdrawn because of the amendment to claim 1. See page 5.

Applicant's arguments, see, filed 10/16/03, with respect to 112 second paragraph rejection have been fully considered and are persuasive. The rejection of claims 1-9, 13-23, 27, 28, 30-34 and 49 has been withdrawn because of the cancellation of the claims 15-23, 27, 28, 30-34 and 49 and the amendment to claim 1. See page 5.

Applicant's arguments, see, filed 10/16/03, with respect to provisional double patenting rejection have been fully considered and are persuasive. The rejection of

claims 15-23, 30-34, and 39 has been withdrawn because of the cancellation of the claims. See page 9.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention encompasses an immunogenic composition comprising a plasmid vector comprising a first nucleotide sequence encoding a RSV G protein or fragment thereof and a control sequence directing expression of said RSV G protein when introduced into host to produce an immune response to said RSV G protein; and operatively linking said first nucleotide sequence to a second nucleotide sequence to increase expression of said RSV G protein in vivo from the vector in the host, wherein said composition produces a balanced Th1/Th2 cytokine profile. The invention lies in the

field of producing an immunogenic composition comprising a plasmid encoding a viral protein (RSV G protein).

In view of the In Re Wands Factors, the as-filed specification does not provide sufficient guidance or evidence for a composition comprising a nucleotide sequence encoding a RSV G protein, wherein said composition produces a balanced Th1/Th2 cytokines profile. At the time of filing, the phenomenon of T helper cell subsets was best characterized in mice (Elgert, Immunology, Wiley-Liss, Inc., First edition, 1996, pages 228-236). The art recognized three T helper subsets that are defined by patterns of cytokine secretion, ability to generate cytotoxic T cells, and ability to generate particular antibody isotypes. For mice, Th1 type cells secrete primarily Il-2, TNF-β and γ-IFN and are associated with cell-mediated immunity and the production of the IgG2a antibody isotypes, whereas Th2 type cells secrete primarily Il-4 and Il-5 and are associated with humoral immunity and the production of the IgG1 antibody isotype. Th0 cells secrete a mixture of cytokines and are thought to be precursors and/or intermediates of Th1 and Th2 type cells. However, in humans, the heterogeneity of cytokine patterns is far more complex, with most T helper cells falling into the Th0 category. While, the as-filed specification working examples show that Balb/C mice immunized intramuscularly or intradermally with the plasmids pXL5 or pXL6 generate cytokine associated with both Th1 and Th2 type responses, g-IFN versus Il-4 and Il-5 (pages 29-30, Fig. 8), the specification does not disclosed the characteristics of the T cells which are secreting these cytokines such they could be called Th1 versus Th2. As noted above, Th0 cells secrete all of these cytokines. Furthermore, as the term "balanced" is not defined by the specification, it is unclear whether a balanced Th1 versus Th2 response refers to equal

numbers of Th1 versus Th2 T cells or equivalent amounts of cytokines associated with Th1 versus Th2 cells or something else entirely.

Furthermore, the prior art at the time the application was filed teaches that several factors, which significantly affect the generation of Th1 versus a Th2 response to an antigen which include, genetics, dose or concentration of antigen, and route of antigen administration (Abbas et al., Nature, Vol. 383, pages 787-793, 1996) and Golding et al., (Am. J. Trop. Med. Hyg., Vol. 50, pages 33-40). The prior art teaches that the concentration of antigen significantly affects the development of Th1 versus Th2 responses such that low antigen concentrations preferentially induce Th1 type responses and high concentrations of antigen induce Th2 type responses (Abbas et al., *supra*). The specification does not provide guidance as to the level of expression of G protein, which would result in both a Th1 and a Th2 type response or provide guidance as to specific cell types, which would present the recombinant antigen in such a way as to result in a particular T helper response. The infectious antigens themselves have also been reported to affect T helper phenotype. For example, intracellular microorganism such as *Salmonella*, *Leishmania*, *Malaria*, and *Listeria* typically induce Th1 type responses, whereas schistosomiasis and *Nippostongyus* typically induce Th2 type responses. A further complicating factor is the genetic background of the infected mammal. The prior art contains numerous reports, which demonstrate the Balb/C mice versus C57Bl/6 mice develop different T helper responses to various pathogens. The nature and route of administration of the antigen is also of concern to the generation of a particular T helper phenotype. Golding teaches that intravenous or intraperitoneal immunization leads to preferential induction of Th1 cells whereas subcutaneous or intramuscular immunization

leads to Th2 cells which may be attributable to the participation of various antigen-presenting cells (Golding, *supra*).

In view of the In Re Wands Factors, the as-filed specification and claims coupled with the art of record at the time the invention was made do not provide sufficient guidance and/or factual evidence to reasonably enable one skilled in the art to make and/or use the claimed invention. One would have to engage in a large quantity of experimentation in order to practice the full scope of the claimed invention based on the breadth of the claims, a significant number of variables affecting the generation of T helper responses, the unpredictability of producing a particular T helper response in any subject for any given antigen, and the lack of sufficient guidance or evidence in the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-9, 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "balanced Th1/Th2 cytokine profile in claims 1-9, 13 and 14 is indefinite. The specification and claims do not define what the metes and bounds of term "balanced" are in relation to a Th1 versus a Th2 response. The claims do not define if this means equivalent number of Th1 or Th2 cells or does it mean that the effector functions of the different cells are equivalent. In addition, as "balanced" is a relative

term, it is unclear what level of difference in the various aspects of a Th1 versus Th2 responses are embraced by the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2 and 5-7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Olmsted et al. (1989, J. Virol., Vol. 63 (1), 411-420) and Simard et al. (Antiviral Research, Vol. 28, pp. 303-315, 1995) in view of Johnson et al. (1987, Proc. Natl. Acad. Sci., Vol. 84, 5625-5629), Wagener et al. (1996, J. Biotech., Vol. 44, 59-65), Norman et al. (June, 1997, Vol. 15 (8), 801-803), and Haddad et al. (July, 1997, Vol. 18, 193-202). Olmsted teaches recombinant vaccinia viruses, which encode either full length or truncated versions of the human RSV G protein, and demonstrates that intranasal administration to rats with the recombinant G protein encoding vaccinia viruses resulted in significant anti-RSV G protein antibody titers (Olmsted et al., page 412, Figure 1, and page 417, Table 1). Olmsted et al. further teaches that the G protein from three strains of RSV, including the Long strain has been sequenced (Olmsted et al., page 411, column 2). Simard also teaches recombinant vaccinia viruses comprising an RSV G protein. Specifically, Simard teaches a fragment corresponding to amino acids 124-203 of the RSV G protein of the Long strain which lacks the trans-membrane region and sequences upstream (Simard et al., page 311, paragraph 2). Simard et al. also teaches that administration to mice with the recombinant plasmid generated significant anti-RSV antibody titers (Simard et al., page310, Table 1). It is further noted that Simard comments that the vaccinia virus is not expected to become a suitable vector for the development of human vaccines (Simard et al., page 313, paragraph 2). Johnson supplements both Olmsted, and Simard by providing the amino acid sequence of the G protein derived from the Long strain of RSV which is 99.1% identical to the nucleic acid sequence encoding applicants SEQ ID NO: 2 (Johnson et al., page 5627, Figure 2).

However, Olmsted and Simard differ from the instant invention in that they utilize replicating vectors i.e. vaccinia virus.

However, at the time the invention was made, Simard suggests that the vaccinia virus is not the vector of choice for use in humans. Wagener supplements Olmsted and Simard by teaching that immunogenic compositions may be safer than live attenuated viruses and that immunogenic compositions comprising a plasmid can be used to induce an immune response similar in scope to attenuated viruses (Wagener et al., page 60, paragraph 2). More specifically, Wagener teaches that administration to mice with a plasmid vector encoding a CMV promoter and comprises a CMV intron A operatively linked to the tissue plasminogen activator (tPA) leader sequence and the SIV gp130 antigen resulted in significant titers of anti-SIV antibodies (Wagener et al., pages 62- 63, and Figures 2+ 3). Norman supports Wagener by teaching that the optimized plasmid vector for gene expression and delivery *in vivo* includes a CMV promoter and enhancer and the CMV IE intron A (Norman et al., page 801, abstract). Haddad further supports Wagener by teaching that the addition of the tPA signal sequence is warranted in order to prevent retention of peptides in the cytoplasm and to ensure proper glycosylation in the ER (Haddad et al., page 201, paragraph, 3).

Therefore, in view of the optimal nature of the plasmid vector taught by Wagener et al. which includes the CMV promoter, CMV intron A, and the tPA signal sequence as taught by Norman and Haddad, and in view of the teachings of Wagener which support the use of plasmid vector over attenuated viral vectors to induce antigen specific antibodies, it would have been *prima facie* obvious to the skilled artisan to use the plasmid vector taught by Wagener to express the RSV G proteins taught by Olmsted,

Johnson, or Simard in order to generate anti-RSV antibody responses *in vivo*. Further based on the well known techniques of molecular biology and the teachings of Olmsted and Simard that the RSV G protein are produced *in vivo*, the skilled artisan would have had a reasonable expectation of success in making a plasmid encoding CMV promoter and comprising a CMV intron A, and the tPA signal sequence and encoding an RSV G protein and using said plasmid to produce an immunogenic composition used to produce antibodies that specifically react with RSV G protein in a mammal.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicants' argue that, "The scientific paper by Li et al describes the problems in the art of an unbalanced cytokine response as well as problems with using vaccinia. From this prior work, a person skilled in the art would draw the conclusion that the RSV G proteins has an inherent basis towards Th2 cytokines production and there would be no expectation that a different result would be obtained using a DNA plasmid vector from that obtained using a vaccinia vector. At the time of this invention it was not known that in vivo expression of the G protein of RSV in a DNA vector would result a shifting of the immune response to a more balanced one regardless of the route of administration, in contrast to the vaccinia work. This result, it is submitted, is an unexpected result." See page 7.

Furthermore, applicants' argue that, "It is submitted that there is nothing in the secondary reference which have been cited to even suggests that this result may be

obtained by replacing the vaccinia virus vector with a plasmid vector, as in the present invention." See page 8.

Applicant's arguments filed 10/16/03 have been fully considered but they are not persuasive.

It is noted that the applicants' did not argue that the claimed invention is patentable over the 103(a) rejection, instead the applicants amended the independent claim with the limitation "balanced Th1/Th2 cytokine profile". The limitation is from an intended use of the product and does not narrow the scope of the product over the prior art. **The applicants' claims are product claims, not method claims.**

Furthermore, the applicants are reminded that the motivation for combining the teachings of the prior art may be different from applicants' motivation to make the disclosed compositions. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). The office has provided motivation for making a plasmid encoding RSV G protein.

Furthermore, regarding the newly added functional language drawn to "a balanced Th1/Th2 cytokine profile," it is noted that a "balanced Th1/Th2 cytokine profile" has been rejected under 35 U.S.C. 112 second paragraph, see above. However, **the applicants' claims are product claims, not method claims**. MPEP 2111.02 states, .. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably

distinguish the claimed invention from the prior art." *In re Casey*, 152 USPQ 235 (CCPA 1967); *In re Otto*, 136, USPQ 458, 459 (CCPA 1963). MPEP further states, "Where the claimed and prior art products are identical or substantially identical in structure or compositions, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation **or obviousness** has been established. MPEP 2112.01 states:

> In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433. See also Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (Claims were directed to a titanium alloy containing 0.2-0.4% Mo and 0.6-0.9% Ni having corrosion resistance. A Russian article disclosed a titanium alloy containing 0.25% Mo and 0.75% Ni but was silent as to corrosion resistance. The Federal Circuit held that the claim was anticipated because the percentages of Mo and Ni were squarely within the claimed ranges. The court went on to say that it was immaterial what properties the alloys had or who discovered the properties because the composition is the same and thus must necessarily exhibit the properties.).

Also, reliance upon inherency is not improper even though a rejection is based on Section 103 instead of 102. *In re Skoner,* 517 F.2d 947, 186 USPQ 80 (CCPA 1975).

Furthermore, in response to applicants' argument that, "From this prior work, a person skilled in the art would draw the conclusion that the RSV G proteins has an inherent basis towards Th2 cytokines production and there would be no expectation that a different result would be obtained using a DNA plasmid vector from that obtained using a vaccinia vector. At the time of this invention it was not known that in vivo expression of the G protein of RSV in a DNA vector would result a shifting of the immune response to a more balanced one regardless of the route of administration, in contrast to the vaccinia work. This result, it is submitted, is an unexpected result." See page 7. "It is submitted that there is nothing in the secondary reference which have been cited to even suggests that this result may be obtained by replacing the vaccinia virus vector with a plasmid vector, as in the present invention." See page 8. Other than the assertion, the applicants provide no guidance and/or evidence to support these assertions. Therefore, applicants' assertions regarding the Li et al., reference and "unexpected results" are not compelling. See MPEP § 716.01(c).

Claims 1-2 and 5-7 remain rejected under 35 U.S.C. 103(a) as being Stott et al. (Journal of Virology, Vol. 60, pp. 607-613, 1986) and Johnson et al. (1987, Proc. Natl. Acad. Sci., Vol. 84, 5625-5629) taken with Simard et al. (Antiviral Research, Vol. 28, pp. 303-315, 1995), Wagener et al. (1996, J. Biotech., Vol. 44, 59-65) and Haddad et al. (July, 1997, Vol. 18, 193-202) in further view of Herrmann et al. (Applicants' IDS, US patent 5,620,896, 1997).

Stott teaches that RSV G protein expressed from a recombinant vector can produced antibodies specific for the RSV G protein (abstract). Stott produced a plasmid

containing a complete cDNA copy of the RSV G gene (page 607). Stott further teaches that the G protein expressed from the recombinant vector induced antibodies in rabbits (page 607). Johnson supplements Stott by providing the amino acid sequence of the RSV G protein derived from the Long strain of RSV which is 99.1% identical to the nucleic acid sequence encoding applicants SEQ ID NO: 2 (Johnson et al., page 5627, Figure 2). However, Stott and Johnson differ from the instant invention that Stott utilized a vaccinia virus vector.

However, at the time the invention was made, Simard suggests that the vaccinia virus is not the vector of choice for use in humans. Wagener supplements Simard by teaching that immunogenic compositions may be safer than live attenuated virus vaccines and that immunogenic compositions induce immune responses similar in scope to attenuated viruses (Wagener et al., page 60, paragraph 2). More specifically, Wagener teaches that administration to mice with a plasmid vector encoding a CMV promoter and comprises a CMV intron A operatively linked to the tissue plasminogen activator (tPA) leader sequence and the SIV gp130 antigen resulted in significant titers of anti-SIV antibodies (Wagener et al., pages 62- 63, and Figures 2+ 3). Haddad further supports Wagener by teaching that the addition of the tPA signal sequence is warranted in order to prevent retention of peptides in the cytoplasm and to ensure proper glycosylation in the ER (Haddad et al., page 201, paragraph, 3). Furthermore, Herrmann provides a control plasmid pCMVIA, a bacterial plasmid that includes SV40 replication origin, the CMV promoter, Intron A and a bovine growth hormone gene that provides a polyadenylation signal (column 5, lines 56-63). Furthermore, Herrmann uses the plasmid, wherein the promoter is operably linked to a nucleotide sequence encoding a rotavirus polypeptide

wherein said rotavirus polypeptide is expressed in a cell of a mammal with said plasmid vector (column 27, lines 39-45).

It would have been *prima facie* obvious for a person of ordinary skill in the art at the time the invention was made to modify the teaching of Stott and Johnson taken with Simard, Wagener, and Haddad in further view of Herrmann to produce an immunogenic composition comprising a RSV G protein to produce an immune response in a mammal. One of ordinary skill in the art would have been motivated to produce this composition since it would facilitate the expression of antibodies specific for the RSV G protein when administered to a mammal.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 10/16/03 have been fully considered but they are not persuasive.

The argument is the basically the same as the argument in the prior rejection 103(a) rejection. Therefore, the argument is not found persuasive for the same reasons as set forth in the examiner's response to the prior 103(a) rejection.

With respect to applicants' argument that, "It is submitted that the Hermann reference adds nothing to other references. This disclosure is limited to a rotavirus and provides no suggestion to provide a plasmid vector containing a promoter and nucleotide sequences encoding RSV G protein," the argument is not found persuasive because one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871

(CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) and because both Stott and Simard provide ample evidence that RSV G proteins are capable of generating antibody responses when expressed *in vivo* using a recombinant vector. Therefore, based on the evidence provided by either Stott or Simard that a viral protein (RSV G protein) expressed by a recombinant viral vector is capable of generating therapeutic levels of antibodies *in vivo*, and the teachings of Wagener et al., that viral proteins expressed from plasmid vectors are also fully capable of generating antibodies *in vivo*, one of ordinary skill in the art would have had a reasonable expectation of success in generating anti-RSV G protein antibodies *in vivo* using a plasmid vector encoding the RSV G protein.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 13 and 14 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable

over claims 1, 6, 7, 10, 11, 13 and 14 of co-pending Application No. 08/896,442. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are directed to making and using an immunogenic composition comprising a plasmid that will not replicate, wherein the plasmid comprises: a first nucleotide sequence encoding a RSV G protein; a promoter sequence operatively linked to said first nucleotide sequence and a second nucleotide sequence encoding the human CMV intron A located between said first nucleotide sequence and said promoter. In addition, both applications are directed to a plasmid vector PXL5 or PXL6.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants request to refer the resolution of this rejection until the instant claims or conflicting claims are patented. See page 10.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE - Art Unit 1635, can be reached at (703) 306-3217.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Brian Whiteman
Patent Examiner, Group 1635